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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/839,779	04/20/2001	Amin I. Kassis	U0381-00001	2010

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EXAMINER

WEBER, JON P

ART UNIT	PAPER NUMBER
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1651

DATE MAILED: 07/08/2003

8

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/839,779

Applicant(s)

KASSIS ET AL.

Examiner

Jon P Weber, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 May 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-22 is/are pending in the application.
- 4a) Of the above claim(s) 4 and 22 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3 and 5-21 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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Status of the Claims

The response with amendments filed 05 May 2003 has been received and entered. Claims 1-22 have been presented for examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restrictions

Newly submitted claim 22 is withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, β -galactosidase, and claim 4 stands withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected group, there being no allowable generic or linking claim because the elected species, phosphatase, was found unpatentable re Griffiths et al. (US 6,361,774) (*vide infra*). Applicant timely traversed the species restriction requirement in Paper No. 5, but elected the group **without** traverse.

This application contains claim 22 drawn to an invention nonelected with traverse in Paper No. 5. A complete reply to the final rejection **must** include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01, for the response to be complete. It is suggested that claim 4 be canceled too.

Claim Rejections - 35 USC § 112

Applicant's arguments with amendments, filed 05 May 2003, have been fully considered and are persuasive. The rejection and objection of claim 5 have been withdrawn.

Claim Rejections - 35 USC § 102 and 103

Claims 1, 5-15 and 17-20 stand rejected under 35 U.S.C. 102(b) as being anticipated by Hansen (US 5,851,527) and claims 1, 5-15 and 20 stand rejected under 35 U.S.C. 102(e) as being anticipated by Griffiths et al. (US 6,361,774).

Claims 1-3 and 5-20 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Hansen (US 5,851,527) in view of Senter et al. (US 4,975,278), Shepard (US 6,495,553) and further in view of Camden (US 6,265,427), Griffin et al. (US 6,156,739) and Horwitz et al. (US 5,854,968).

It is argued that neither Hansen nor Griffiths et al. can meet the newly added limitation of "trapped within the extracellular space of the solid tumor". It is urged that several disclosures in Hansen indicate that the compounds are in some way deposited on the cell membranes and may even permeate into the cells of the solid tumor.

The conclusion re permeating the cells is completely unwarranted. Nothing in Hansen suggests that this is the case. In Hansen, it is preferred to select prodrugs for which there is not an endogenous hydrolyzing enzyme in the host. The appropriate enzymes are conjugated to antibodies that recognize antigens on the membrane surface of tumor cells. In this manner, the desired enzymes are targeted to the extracellular surface of the tumor cells. In Hansen or Griffiths et al., as evidenced by the quoted portions and elsewhere, the prodrugs permeate the interstitial fluid of the tumor. Reaction of the prodrug with enzymes on the membrane surface of the tumor cells will result in the precipitation of the drug on the membrane surface of tumor cells lining the interstitial regions. At page 5, line 29 to page 6, line 1 of the instant disclosure (the

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only place where there is support for the newly added limitation) the extracellular space and the interstitial space as said to be the same thing. Hence, a correct reading of Hansen or Griffiths et al. reveals that the drugs are precipitated within the interstitial space of the tumor. According to *In re Sussman*, 141 F. 2d 267, 60 U.S.P.Q. 538 (CCPA 1944), "since the steps are the same, the results must inherently be the same unless they are due to conditions not recited in the claims." In the particular case, Applicants are claiming an invention employing the **same process steps** but the products are **alleged to be different**.

Applicant's arguments filed 05 May 2003 have been fully considered but they are not persuasive. The rejections under 35 U.S.C. 102 and 103 are adhered to for the reasons of record and the additional reasons above.

Claim Rejections - 35 USC § 103

Claim 1, 5-15 and 20-21 are now rejected under 35 U.S.C. 103(a) as being unpatentable over Hansen (US 5,851,527) and Griffiths et al. (US 6,361,774) in view of Griffin et al. (US 6,156,739), Christenson (US 4,107,285) and Padia (US 5,756,502).

Newly added claim 21 is drawn to use of a radio- or boron-labeled quinazolinone dye in the claimed method.

The teachings of Hansen (US 5,851,527), Griffiths et al. (US 6,361,774) and Griffin et al. (US 6,156,739) were discussed in the Office action of 03 February 2003. Neither Hansen (US 5,851,527) nor Griffiths et al. (US 6,361,774) disclose radio- or boron-labeled quinazolinone dye.

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Christenson (US 4,107,285) disclose that it is known to radiolabel quinazolinone dye, e.g., methaqualone, with ^{125}I .

Padia (US 5,756,502) that it is known to radiolabel quinazolinone dye of formula I therein with ^{125}I (column 6, lines 26-29).

A person of ordinary skill in the art at the time the invention was made would have been motivated to substitute radiolabeled quinazolinone dye of Christenson (US 4,107,285) and Padia (US 5,756,502) for the non-radiolabeled quinazolinone dye of Griffin et al. (US 6,156,739) in the method of Hansen (US 5,851,527) and Griffiths et al. (US 6,361,774) because the radiolabel would make the quinazolinone more effective in the method of Hansen (US 5,851,527) and Griffiths et al. (US 6,361,774) as disclosed therein. The quinazolinones of Griffin et al. are made soluble by phosphorylation for improved delivery to the target site. The dyes are converted to the insoluble active form by phosphatase. Hansen (US 5,851,527) and Griffiths et al. (US 6,361,774) broadly teach that any suitable drug can be used.

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to select the radiolabeled quinazolinone because of its known insolubility for use in the method of Hansen (US 5,851,527) and Griffiths et al. (US 6,361,774).

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon P Weber, Ph.D. whose telephone number is 703-308-4015. The examiner can normally be reached on daily, off 1st Fri, 9/5/4.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Wityshyn can be reached on 703-308-4743. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Jon P Weber, Ph.D.
Primary Examiner
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JPW
July 7, 2003